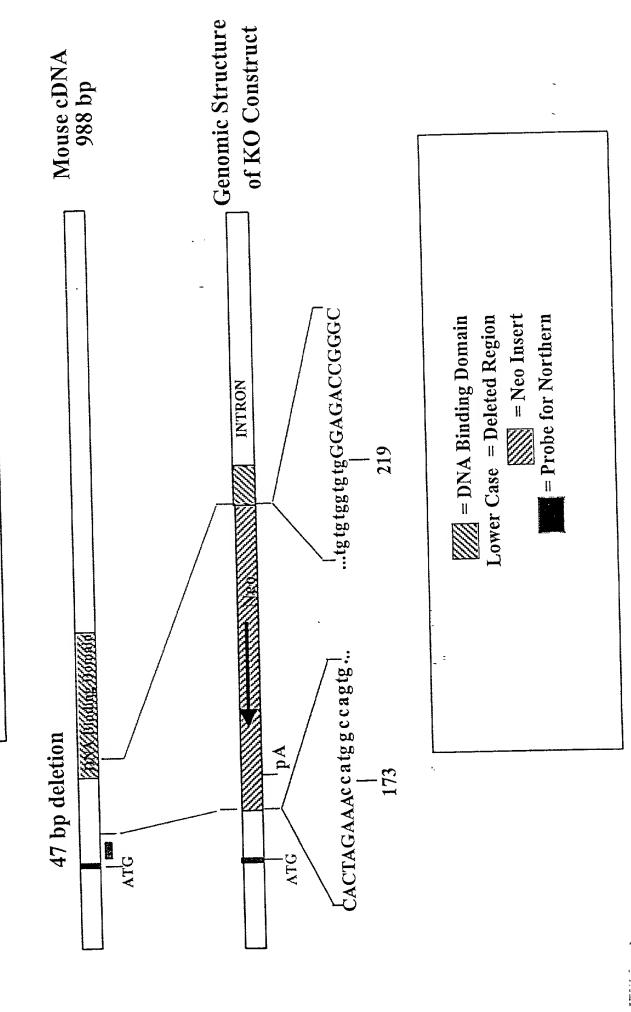
### Figure 1

# CAR KNOCK-OUT CONSTRUCT



### FIGURE 2

### Section A.

### Section B.

....aaagaggteatcaggettggeageaagtgeetttgeetaeegagtetttaeaeeageteeaeegtggtttttgagaeagteteeeaetgg ggttctaggaattaaactcggctctcggtgcttatatagtgagtactttacagagggagtcaccttgccagcacctagaattcacttttattcatat ctcagaaggcaagagctccttgcagaggatttaacctcaattcctagtactcaacttgccagctcataactgcctataactctagtcccagaag ctctcccattgtttcctggcttattcaggatccatgcaaaaaggggagtgtagatttagcctaaagctcacccacagggaaatcctccaggagt eccaccccacacccagg totttgcctgggtccagagtctgggtcctacctacatatggcaccgaggatacctagaggccccatgcaagagaaggcccttgttttccaggcactaaggaccgcagtccctaattcctggcagttcctgagatctcaaggaaagcagggtcagcga caaaaagcaacatttttgcttttaatgtcctcagtgctggggagcccggtgtcaggctgggcagtcttgggaagagattctgtagaggagaga gaagagagtcctatggcccagtgctgattctcaactcctcccacattcaggagaccATGACAGCTATGCTAACACTAG AAA*CCATGGCCAGTGAAGAAGAATATGGGCCGAGGAAC<u>TGTGTGTGTGTGT*GGAGACC</u> <u>GGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGAGGGCTGCAAGGGCTTCTTCA</u> <u>Ggtgaatgetteeteeceaacagaaacaaceegacatttetateagteeacetttaaacaetggtaeaceteeaagttataateetettgeag</u> ctaagctgcactgccagtgtctagcactctcaatcttgctgaccacaacgcagtgtgaaactggtgacctaatgacaaggcaggttaaccat ttgtcccagagacagagcctaagagtcaagaacacttgtgtagcacacactacctgcaaagcaccgagatgattgccacacgagggttcct gagtaacettgtgttctcatgaaaacgetccaactacetctgaagacetttgagcacagetcagatgagtctgttgttaaatcgatcc.....

### Section C.

5β-Pregnan-3,20-dione is an hCAR Agonist

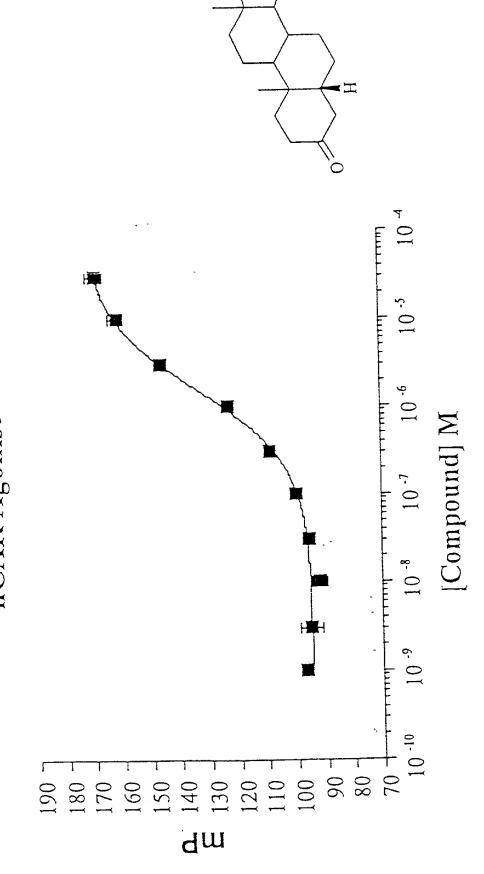
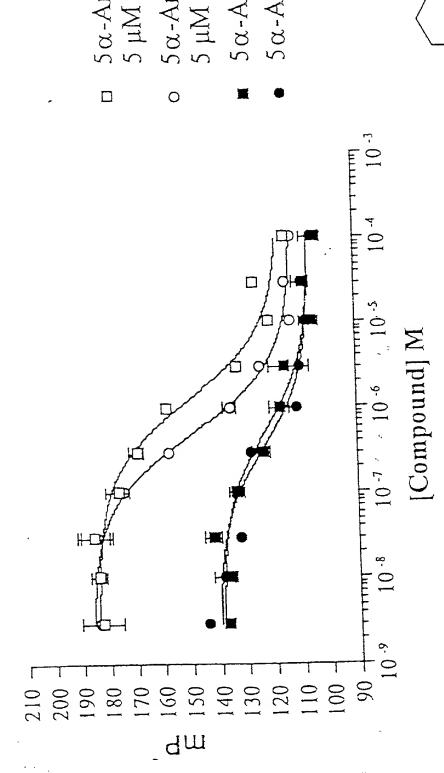


Figure 3

## Figure 4

Androstanes are hCAR Antagonists



$$_{\rm B}$$
 5 $\alpha$ -Androst-16-en-3  $\alpha$ -ol + 5  $\mu M$  5  $\beta$ -Pregnan-3,20-dione

 $1.2~\mu M$ 

IC 50

$$5\alpha$$
-Androstan-3  $\alpha$ -ol +  $5\mu M$  5  $\beta$ -Pregnan-3,20-dione

480 nM

$$5\alpha$$
-Androst-16-en-3  $\alpha$ -ol  $5\alpha$ -Androstan-3  $\alpha$ -ol

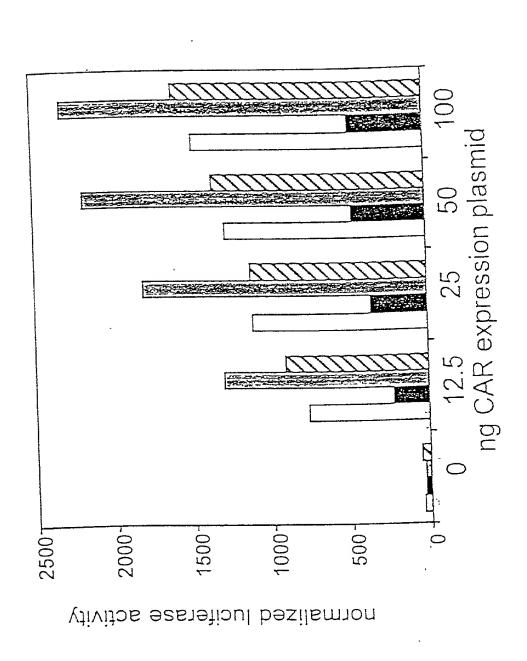
340 nM

530 nM

$$5\alpha$$
-Androstan- $3\alpha$ -ol  $5\alpha$ -And

$$5\alpha$$
-Androst-16-en- $3\alpha$ -ol

FIGURE 5



5β- pregnan-3,20-dione

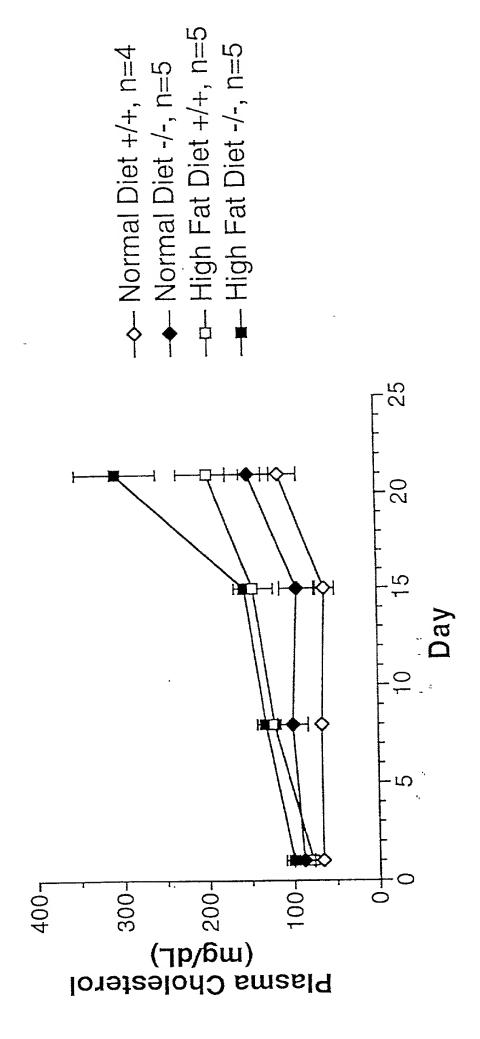
I 5β-pregnan-3,20-dione

 $\alpha$  5 $\alpha$ -androstan-3 $\alpha$ -ol

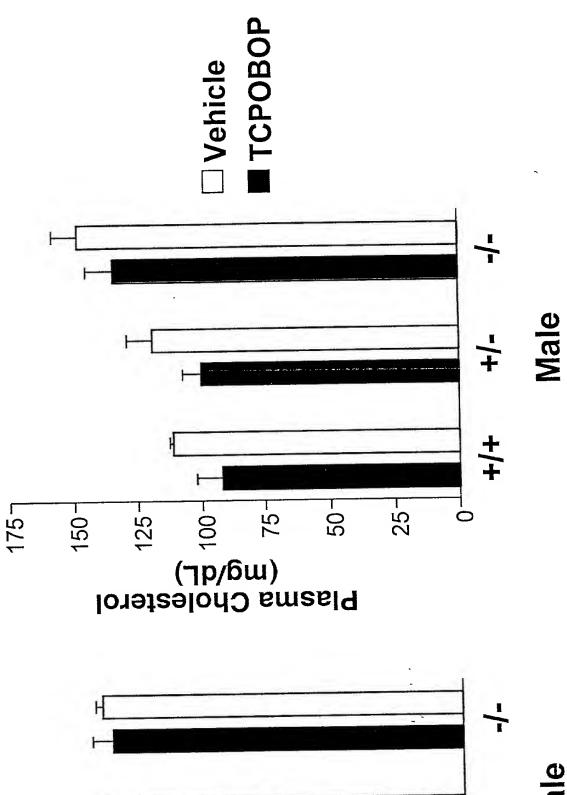
5α-androstan-3α-ol

□ vehicle





Normal diet = Picolab 5053 (containing 4% fat) High Fat diet = Picolab 5053 (containing 1.25% cholesterol and 10% fat)



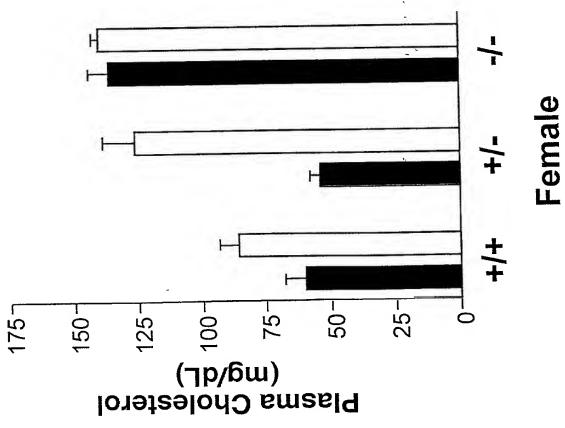
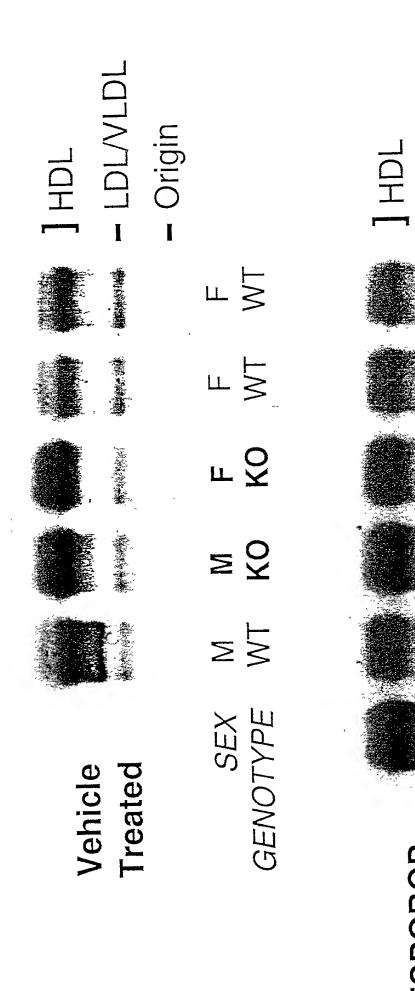


FIGURE 8



- LDL/VLDL

Origin

H W

т 8

≥ ♀

Σ×

 $\Sigma \stackrel{\vdash}{\geqslant}$ 

SEX GENOTYPE

TCPOBOP Treated

